

AMENDMENTS TO THE CLAIMS

1. (Currently amended) A recombinant mutant allergen, ~~characterised in that it is a mutant~~ of a naturally occurring allergen,

said naturally occurring allergen selected from the group consisting of Fagales group 1 allergens, Vespidae antigen 5 allergens, house dust mite group 1 allergens, house dust mite group 2 allergens and grass group 5 allergens and comprising wherein the mutant allergen has at least four primary mutations, which each reduce the specific IgE binding capability of the mutated allergen as compared to the IgE binding capability of the said naturally occurring allergen,

wherein each primary each of said at least four mutations being is a substitution of one surface-exposed amino acid residue with another residue, which does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates,

wherein each primary each of said at least four mutations being is spaced from each other ~~primary mutation~~ by at least 15 Å, and

wherein the primary mutations are placed in such a manner that said mutant allergen comprising at least one circular surface region with an area of 800 Å² that comprises no mutation.

2. (Currently amended) A recombinant mutant allergen according to claim 1, wherein the ~~primary each of said at least four mutations are~~ is spaced ~~from each other by~~ between about 20 to 30 Å.

3. (Currently amended) A recombinant mutant allergen according to claim 1 which comprises at least five mutations in total, which each reduces the specific IgE binding capability of the mutated allergen as compared to the IgE binding capability of said naturally occurring allergen,

each of said at least five mutations in total being a substitution of one surface-exposed amino acid residue with another residue, which does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates, and

at least two of said at least five mutations in total being spaced within 15 Å of each other comprising a number of secondary mutations, which each reduce the specific IgE-binding

~~capability of the mutated allergen as compared to the binding capability of the said naturally occurring allergen, wherein each secondary mutation is a substitution of one surface-exposed amino acid residue with another residue, which does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates, wherein the secondary mutations are placed outside the said circular region.~~

4. (Currently amended) A recombinant mutant allergen according to claim 1, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen has a solvent accessibility of above 20 %.

5. (Currently amended) A recombinant mutant allergen according to claim 1, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen is conserved with more than 70 % identity in all known homologous proteins within the species from which said naturally occurring allergen originates.

6. (Currently amended) A recombinant mutant allergen according to claim 1, which essentially has the same α -carbon backbone tertiary structure as said naturally occurring allergen.

7. (Currently amended) A recombinant mutant allergen according to claim 1, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic genus from which said naturally occurring allergen originates.

8. (Currently amended) A recombinant mutant allergen according claim 1, characterised in that the specific IgE binding to the mutated allergen is reduced by at least 5%.

9. (Currently amended) A recombinant mutant allergen according to claim 6, characterised in that when comparing the α -carbon backbone tertiary structures of the mutant and

the naturally occurring allergen molecules, the average root mean square deviation of the atomic coordinates is below 2Å.

10. (Currently amended) A recombinant mutant allergen according to claim 1, characterised in ~~that~~ said circular surface region comprises atoms of 15-25 amino acid residues.

11. (Currently amended) A recombinant mutant allergen according to claim 1, characterised in that the surface-exposed amino acid residues are ranked with respect to solvent accessibility, and that one or more amino acids among the more solvent accessible ones are substituted.

12. (Currently amended) A recombinant mutant allergen according to claim 1, characterised in that the surface-exposed amino acid residues are ranked with respect to degree of conservation in all known homologous proteins within the species from which said naturally occurring allergen originates, and that one or more amino acids among the more conserved ones are substituted.

13. (Currently amended) A recombinant mutant allergen according to claim 1, wherein the mutant allergen is a non-naturally occurring allergen.

14. (Currently amended) A recombinant mutant allergen according to claim 1 comprising from 5 to 20 primary mutations that reduce the specific IgE binding capability of the mutated allergen as compared to the IgE binding capability of said naturally occurring allergen, each of said 5 to 20 mutations being a substitution of one surface-exposed amino acid residue with another residue, which does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates, and
each of said 5 to 20 mutations being spaced from each other by at least 15 Å.

15. (Currently amended) A recombinant mutant allergen according to claim 3, which comprises at least 8 total mutations and wherein each of said at least four mutations spaced from each other by at least 15 Å is spaced within 15 Å of 1 to 4 of said at least 8 total mutations characterised in that the mutant allergen comprises from 1 to 4 secondary mutations per primary mutation.

16. (Currently amended) A recombinant mutant allergen according to claim 1 wherein said naturally occurring allergen is a grass group 5 allergen selected from the group consisting of Lol p 5, Phl p 5, Poa p 5 and Sec c 5. -characterised in that one or more of the substitutions is carried out by site-directed mutagenesis.

17. (Currently amended) A recombinant mutant allergen according to claim 1 wherein said naturally occurring allergen is a house dust mite group 2 allergen selected from the group consisting of Der p 2, Der f 2 and Lep d 2. -characterised in that one or more of the substitutions is carried out by DNA shuffling.

18. (Currently amended) A recombinant mutant allergen according to claim 1 wherein said naturally occurring allergen is a Fagales group I allergen selected from the group consisting of Bet v 1, Aln g 1, Cor a 1 and Car b 1. -characterised in that it is a mutant of an inhalation allergen.

19. (Currently amended) A recombinant mutant allergen according to claim 1 wherein said naturally occurring allergen is a Vespidae antigen 5 allergen selected from the group consisting of Ves v 5 and Pol a 5. -18,characterised in that it is a mutant of a pollen allergen.

20. (Currently amended) A recombinant mutant allergen according to claim 1 wherein said naturally occurring allergen is a house dust mite group 1 allergen selected from the group consisting of Der p 1, Der f 1 and Lep d 1. -19characterised in that it is a mutant of a pollen allergen originating from the taxonomic order of Fagales, Oleales or Pinales.

21. (Currently amended) A recombinant mutant allergen according to claim 18 20, characterised in that it is a mutant of Bet v 1.

22. (Currently amended) A recombinant mutant allergen according to claim 21, characterised in that one or more of the substitutions is selected from the group consisting of V-2, D-72, E-87, K-129, E-60, N-7, K-65, P-108, N-159, D-93, K-123, K-32, D-125, R-145, D-109, E-127, Q-36, E-131, L-152, E-6, E-96, D-156, P-63, H-76, E-8, K-134, E-45, T-10, V-12, K-20, S-155, H-126, P-50, N-78, K-119, V-2, L-24, E-42, N-4, A-153, I-44, E-138, G-61, A-130, R-70, N-28, P-35, S-149, K-103, Y-150, H-154, N-43, A-106, K-115, P-14, Y-5, K-137, E-141, E-87 and E-73.

23 and 24. (Cancelled)

25. (Cancelled) ~~A recombinant mutant allergen according to claim 18, characterised in that it is a mutant of a house dust mite allergen.~~

26. (Cancelled) ~~A recombinant mutant allergen according to claim 25, characterised in that it is a mutant of a mite allergen originating from Dermatophagoides.~~

27. (Cancelled)

28. (Cancelled) ~~A recombinant mutant allergen according to claim 18, characterised in that it is a mutant of an animal allergen.~~

29-34. (Cancelled)

35. (Currently amended) A pharmaceutical composition comprising the recombinant mutant allergen according to claim 1 and at least one of a pharmaceutically acceptable carrier, excipient, or adjuvant.

36. (Cancelled)

37. (Currently amended) A composition comprising two or more recombinant mutant allergens according to claim 1, wherein each of said two or more recombinant mutant allergens respectively comprises at least one ~~primary~~ mutation among said at least four mutations spaced at least 15 Å from each other that is at least 15 Å from any other mutation that is not within a radius of 15 Å from a secondary mutation and which is absent in at least one other of said two or more recombinant mutant allergens.

38. (Currently amended) A composition according to claim 37 comprising 2-12 recombinant mutant allergens variants.

39. (Previously presented) A composition according to claim 37 further comprising at least one of a pharmaceutically acceptable carrier, excipient, or adjuvant.

40-63. (Cancelled)

64. (Currently amended) A recombinant mutant allergen according to claim 1 comprising at least one T cell epitope capable of stimulating a T cell clone or T cell line specific for the naturally occurring allergen.

65. (Cancelled)

66. (Currently amended) The recombinant mutant allergen of claim 2 wherein said at least four ~~the primary~~ mutations are spaced from each other by at least 25 Å.

67. (Currently amended) The recombinant mutant allergen of claim 66 wherein said at least four ~~the primary~~ mutations are spaced from each other by at least 30 Å.

68. (Currently amended) The recombinant mutant allergen according to claim 4, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen has a solvent accessibility of above 30 %.

69. (Currently amended) The recombinant mutant allergen according to claim 68, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen has a solvent accessibility of above 40 %.

70. (Currently amended) The recombinant mutant allergen according to claim 69, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen has a solvent accessibility of above 50 %.

71. (Currently amended) A recombinant mutant allergen according to claim 5, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen is conserved with more than 80 % identity in all known homologous proteins within the species from which said naturally occurring allergen originates.

72. (Currently amended) A recombinant mutant allergen according to claim 71, wherein at least one of the surface-exposed amino acids to be substituted in the naturally occurring allergen is conserved with more than 90 % identity in all known homologous proteins within the species from which said naturally occurring allergen originates.

73. (Currently amended) A recombinant mutant allergen according to claim 7, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic subfamily from which said naturally occurring allergen originates.

74. (Currently amended) A recombinant mutant allergen according to claim 73, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic family from which said naturally occurring allergen originates.

75. (Currently amended) A recombinant mutant allergen according to claim 74, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the

same position in the amino acid sequence of any known homologous protein within the taxonomic superfamily from which said naturally occurring allergen originates.

76. (Currently amended) A recombinant mutant allergen according to claim 75, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic legion from which said naturally occurring allergen originates.

77. (Currently amended) A recombinant mutant allergen according to claim 76, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic suborder from which said naturally occurring allergen originates.

78. (Currently amended) A recombinant mutant allergen according to claim 77, wherein each amino acid residue to be incorporated into the mutant allergen does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic order from which said naturally occurring allergen originates.

79. (Currently amended) A recombinant mutant allergen according claim 8, characterised in that the specific IgE binding to the mutated allergen is reduced by at least 10%.

80. (Currently amended) A recombinant mutant allergen according to claim 14 comprising from 6 to 15 primary mutations that reduce the specific IgE binding capability of the mutated allergen as compared to the IgE binding capability of the said naturally occurring allergen, each of said 6 to 15 mutations being a substitution of one surface-exposed amino acid residue with another residue, which does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates, and each of said 6 to 15 mutations being spaced from each other by at least 15 Å.

81. (Currently amended) A recombinant mutant allergen according to claim 80 comprising from 7 to 12 ~~primary~~ mutations that reduce the specific IgE binding capability of the mutated allergen as compared to the IgE binding capability of the said naturally occurring allergen, each of said 7 to 12 mutations being a substitution of one surface-exposed amino acid residue with another residue, which does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates, and
each of said 7 to 12 mutations being spaced from each other by at least 15 Å.

82. (Currently amended) A recombinant mutant allergen according to claim 81 comprising from 8 to 10 ~~primary~~ mutations that reduce the specific IgE binding capability of the mutated allergen as compared to the IgE binding capability of the said naturally occurring allergen, each of said at said 8 to 10 mutations being a substitution of one surface-exposed amino acid residue with another residue, which does not occur in the same position in the amino acid sequence of any known homologous protein within the taxonomic species from which said naturally occurring allergen originates, and
each of said 8 to 10 mutations being spaced from each other by at least 15 Å.

83. (Currently amended) A composition according to claim 38 comprising 3-10 recombinant mutant allergens variants.

84. (Currently amended) A composition according to claim 83 comprising 4-8 recombinant mutant allergens variants.

85. (Currently amended) A composition according to claim 84 comprising 5-7 recombinant mutant allergens variants.